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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,072	03/23/2006	Hiroshi Oda	P29558	6970

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EXAMINER	
MAASHO, KERIMA K	
ART UNIT	**PAPER NUMBER**
1645	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/573,072	ODA ET AL.	
	Examiner	Art Unit	
	Kerima Maasho	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/21/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15 are pending in this application.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01.

The methods as claimed are incomplete, they only recite measuring Lipocalin-type prostaglandin D synthase (L-PGDS), but does not provide a correlation step or indicate what levels would detect pregnancy-induced hypertension. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Claims 1-14 are vague and indefinite because the methods as claimed are so broad and don't recite a complete method.

Claims 2, 3, and 7 are vague and indefinite because they recite the term "normal pregnant women". What is encompassed by the term "normal", e.g. does this refer to a

normal weight, no gestational diabetes, not advanced maternal age, etc? Does the term mean to convey a pregnant woman not inflicted with pregnancy-induced hypertension? Clarification and correction is required.

Claim 4 is vague and indefinite because it is directed to determining the severity of pregnancy-induced hypertension, but provides no values which indicate what is considered 'mild', 'high risk', etc.

Claim 8 is vague and indefinite because it is unclear what is meant by "evaluating fetus and placental function". What type of function is being evaluated? E.g. blood flow, fetal heart, fetal brain activity, etc? Clarification and correction is requested.

Claims 9-14 recite the methods measure the level of L-PGDS in a body fluid (blood or urine) by an immunological assay method. There are many immunological assay methods, which in particular are the applicants referring to? The metes and bounds of the claimed methods are not clear. A claim is indefinite where it merely recites a process without any active, positive steps delimiting how this process is actually practiced.

Claim Rejections - 35 USC § 112-enablment

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case the applicants claim a method of detecting pregnancy-induced hypertension by measuring the level of L-PGDS in body fluid samples. The disclosure does not enable for the detection of pregnancy-induced hypertension but rather the detection of L-PGDS in body fluid samples of a patient with pregnancy-induced hypertension. The disclosure does not teach a particular method that would detect pregnancy-induced hypertension as opposed to other onsets of hypertension, therefore, the method for detecting or predicting or determining the severity of pregnancy-induced hypertension is not enabled.

The specification is also not enabling for a method of "evaluating a fetus and a placental function". All the support examples of the instant invention relate to detecting L-PGDS levels in the serum or blood of a pregnant woman and provide no working examples with samples taken from a fetus or the placenta. It is not clear how detecting the level of L-PGDS in a body fluid sample collected from a pregnant woman who has developed PIH can be used to evaluate fetus and placental function as claimed. In the disclosure it is stated that the "evaluation of a fetus and placental functions" means evaluation of whether or not placental functions for supplying nutrition and oxygen to a fetus decrease or means to evaluate whether or not any injury such as organ damage occurs in the fetus. When the L-PGDS level in a body fluid sample is low, the fetus and placental

functions are evaluated to be in a good state. When the same is high, the fetus and placental functions are evaluated to be in a sub-optimal state. It is well known in the art that hypertension in the pregnant woman affects the development of the placenta, which is important for the nourishment and growth of the fetus. Low amniotic fluid levels and/or intrauterine growth restriction could have adverse effect on the fetus. While the detection of the levels of L-PGDS is indicative of the state of the mother thereby the dangers for the fetus it is by no means an evaluation of a fetus and placental function.
The state of the art: L-PGDS is normally present in various organs (such as CNS, retina and genital organs) and is found in body fluids (such as serum, urine and amniotic fluids) Manya et al 2000, J Biochem, vol 127, pp 1001-11. The levels of L-PGDS are reportedly higher due to hypertension in patients with cardiovascular injuries, kidney injuries and in some pregnancies (Eguchi et al 1997, PNAS, vol 94, pp 14689-94 and Hirawa et al 2002, Hypertension, vol 39, pp 449-54). There is thus far no evidence in the prior art to indicate that hypertension-induced levels of L-PGDS are any different in pregnancy from that of renal dysfunction or heart conditions.

Therefore, only the method of detecting L-PGDS, and not the full breadth of the claims are enabled in 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Oda et al (Clinical Chemistry, 2002, vol 48, pp 1445-53) or Melegos et al (Clinical Chemistry, 1996, vol 42, pp 1984-91).

Claim 15 refers to a kit for detecting human L-PGDS. The term "for detecting pregnancy-induced hypertension" in the claim is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

Oda et al teach the development and evaluation of a Practical ELISA for human L-PGDS detection in the urine using monoclonal antibodies 1B7 and 7F5 as in the present invention. Oda et al's teaching anticipates the kit of the instant invention.

Melegos et al teach the development of a quantitative and sensitive assay using anti-human L-PGDS monoclonal antibodies 1B7 and 7F5 to detect L-PGDS in human tissue extracts and fluids. Melegos et al's teaching anticipates the kit of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 refer to a method of measuring the level of human lipocalin-type prostaglandin D synthase in a body fluid sample. Claims 9-14 refer to a method of measuring L-PGDS by an immunological assay. Claim 15 refers to a kit containing L-PGDS antibody.

4. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirawa et al (Hypertension 2002, vol 39, pp 449-54) in view of Edelstam et al (Scand J

Clin Lab Invest 2001, vol 61, pp 583-91) and Oda et al (US Patent 6,461,827) in light of http://en.wikipedia.org/wiki/Pre-eclampsia.

Hirawa et al teach that serum L-PGDS values and urinary excretions of L-PGDS are much higher in patients with essential hypertension than those in normotensive subjects, even when the patients with essential hypertension exhibit apparently normal renal function (see abstract and last paragraph of Introduction). Which means that regardless of the source of the hypertension there is an increased level of L-PGDS in hypertensive patients. Hirawa et al further teach that hypertension coupled with renal injuries is associated with further increased L-PGDS concentration in sera and in urine. While Hirawa et al teach L-PGDS as a marker for hypertensive conditions they do not specifically teach this in pregnancy.

Edelstam et al teach the importance of developing a reference value assay by using diagnostic parameters of normal pregnant women to determine progressive pre-eclampsia in pregnancy-induced hypertension (p 583 and 584). Edelstam et al while teaching a method for detection of lipocalin in pregnancy-induced hypertensive women they do not teach the measurement of L-PGDS. Pre-eclampsia may develop at varying times within pregnancy and are classified as a medical condition where hypertension arises in pregnancy (pregnancy-induced hypertension) (http://en.wikipedia.org/wiki/Pre-eclampsia). Edelstam et al discuss the need to have a diagnostic tool for the diagnosis of progressive pre-eclampsia during pregnancy and while teaching a method to

determine progressive pre-eclampsia by measuring human neutrophilic lipocalin Edelstam et al do not teach the determination of lipocalin-type prostaglandin D synthase in their assay.

Oda et al teach a method of detecting or predicting ischemic disorder by using as an indication the concentration of human lipocalin-type prostaglandin D synthase in body fluid samples from subjects. Oda et al further teach that the method used comprises comparing the L-PGDS concentration in the body fluid samples from normal subjects a reference, thereby detecting or predicting the ischemic disorders. Reference value of the L-PGDS for each type of body fluid sample such as blood and urine as in the instant invention was established. Oda et al teach an immunological assay such as ELISA for the method of detecting, as well as predicting subjects at high risk of getting ischemic disorder. Furthermore, Oda et al teach a kit which contains an anti-human L-PGDS antibody. While Oda et al teach all the limitations of the above claims in the instant invention they do not teach the method of detecting L-PGDS in samples from individuals with pregnancy-induced hypertension.

Hirawa et al's teaching indicates that L-PGDS regardless of the source is found to be present in the serum and urine of hypertensive patients, Edelstam et al teach the importance of setting a reference value for the diagnosis of markers for pre-eclampsia and Oda et al teach the development of methods and kits for the detection of L-PGDS in blood and in urine.

Taken together, the knowledge of the presence of L-PGDS in the serum and urine of hypertensive patients, with the information of the importance of employing a reference value in pregnant conditions to delineate a cut off value for determining a specific marker, and the working example of developing a method and kit for the detection of L-PGDS in blood and urine samples gives the motivation to one skilled in the art to combine the above teachings with a reasonable expectation of success.

Therefore, it would have been obvious to combine the above teachings to develop a method of detecting pregnancy-induced hypertension by measuring L-PGDS in a body fluid sample as in the instant invention. Therefore, the teachings of Hirawa et al, Edelstam et al and Oda et al are obvious over the above claims of the instant invention.

Claims 8 and 12 refer to a method of evaluating a fetus and a placental function through the detection of L-PGDS, however the method consist of detecting the level of L-PGDS from blood and urine as for the rest of the claims therefore they are unpatentable over Hirawa et al, Edelstam et al and Oda et al as above.

Conclusion

Claims 1-15 are rejected as explained above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kerima Maasho whose telephone number is 571-270-

3055. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Graser/

Primary Examiner, Art Unit 1645

Patent Examiner, Art Unit 1645